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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,643	03/20/2002	Richard Fayrer-Hosken	235.00300101	1109

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EXAMINER	
SZPERKA, MICHAEL EDWARD	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 09/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/019,643	FAYRER-HOSKEN ET AL.	
	Examiner	Art Unit	
	Michael Szperka	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4,6,12-15,17-19,21,23,27-29 and 41-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,6,12-15,17-19,21,23,27-29 and 41-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Please note that the examiner of record for your application has changed. To aid in paper matching, please address all future correspondence to Michael Szperka, Art Unit 1644, Technology Center 1600.

Applicant's response and amendments received July 12, 2006 are acknowledged.

Claims 4, 27, and 29 have been amended.

Claims 4, 6, 12-15, 17-19, 21, 23, 27-29, and 41-47 are pending.

Claims 4, 6, 12-15, 17-19, 21, 23, 27-29, and 41-47 are under examination as they read on methods of administering immunogenic compositions comprising avian and non-avian zona pellucida proteins.

Claim Rejections - 35 USC § 102

2. The rejection of claims 4, 6, 12-15, 17-18, 21, 23, 27-29, 42 and 44-47 under 35 U.S.C. 102(b) as being anticipated by US Patent No. 5,656,488 (reference found in IDS of 2-14-03) has been withdrawn in light of applicant's claim amendments received July 12, 2006.

Specifically, the independent claims have been amended to recite that the administered composition comprises avian and non-avian zona pellucida proteins, a limitation not taught in the '488 patent.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. The rejection of claims 4, 17-19 and 43 under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,656,488 in view of US Patent 5,686,292 has been withdrawn in light of applicant's claim amendments received July 12, 2004.

Specifically, neither the '488 nor the '292 patent teach the administration of a composition comprising avian and non-avian zona pellucida proteins, a limitation added to all independent claims by applicant's amendments received July 12, 2006.

The following are new grounds of rejection:

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 4, 6, 12-15, 17, 18, 21, 23, 28, 29, and 41-47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Independent claim 4 recites a method for treating diseases "related to" egg production or egg laying. How are these diseases related since any disease can be "related to" something else in some manner? Are the diseases caused by egg production or is some other mechanism involved? Dependent claim 6 recites limitations that address some of these issues, but such limitations are not present in any other claim that depends directly or indirectly from claim 4.

Dependent claim 6 recites "cloacal problems" and "undesirable behavior as a result of reproductive activity or reproductive problems." What are cloacal problems? What behaviors are undesirable, and how do these behavior result from reproductive activity or problems? Is sexual promiscuity an undesirable behavior that results from reproductive activity? Do birds exhibit depression as a result of infertility and lack of egg production?

Claims 28 and 47 recite "wherein the immunogenic conjugate is dually functional" but the two functions of the immunoconjugate are not recited. As such, what are the functions that the immunocongugate comprises? It is noted that the specification exemplifies, but does not define, "dually functional" conjugates from line 20 of page 11 to line 15 of page 12. Therefore, a skilled artisan is not apprised of the metes and bounds of the claimed invention.

Claim 29 recites "A method for affecting the reproductive system of a bird" by administering a composition, but the claim does not recite the effect caused by said administration. How is the reproductive system altered by performing applicant's method? Is reproductive activity increased, decreased, eliminated, or altered in some unspecified way by applicant's method?

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

8. Claims 4, 6, 12-15, 17-19, 21, 23, 27-29, and 41-47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant has claimed a method for treating or preventing reproductive diseases and disorders by administering a composition comprising avian and non-avian zona pellucida (ZP) proteins to birds. The specification prophetically teaches that

administering said composition induces the production of antibodies that bind to the zona pellucida proteins present on eggs (example VIII), and that the presence of anti-ZP antibodies in an animal cause either temporary or permanent sterility (see particularly the paragraph spanning pages 17 and 18). Diseases taught by the specification as being amenable to prevention or treatment by the instant claimed methods include those recited in dependent claim 6.

Prevention requires that applicant's claimed method works in 100% of animals 100% of the time. As stated above, the specification does not provide a working example wherein a composition comprising avian and non-avian ZP was administered to a bird, and as such there is no evidence of record that performing applicant's method can prevent any reproductive disease.

Administration of an immunogenic composition comprising avian and non-avian ZP proteins as per applicant's method elicits the production of antibodies that bind the ZP proteins present in the ovaries of the immunized bird. ZP proteins are important for the binding of sperm to eggs. The presence of these antibodies can have many effects, ranging from inhibition of sperm binding to eggs due to steric hindrance up to autoimmune-mediated destruction of ovarian tissue (Mahi-Brown et al., Birth Control Vaccines, 1995, pages 41-61, see entire document, and see the paragraph spanning pages 17 and 18 of the instant specification). Given that administration of ZP proteins to an animal often leads to ovarian autoimmune disease, it appears that applicant's method causes reproductive disease rather than prevents or treats reproductive diseases.

Further, a review of the art indicates that many of the recited reproductive diseases are caused by infection with bacterial, viral or other pathogenic organisms. Specifically, Shivaprasad teaches that fowl typhoid and pillorum disease are bacterial diseases that cause peritonitis and salpingitis in chickens (Rev. Sci. Tech. 2000, 19:405-424, see particularly the abstract). Salpingitis can also be caused by infections with *Tetratrichomonas, E. coli*, and *Pasteurella multocida* (Crespo et al., J.Vet Diagn. Invest. 2001, 13:240-245, see particularly page 240). Egg-binding is caused by many factors, including lack of tonus or weak tonus of the oviduct or cloacal musculature,

pelvic deformations, eggs that are too large, eggs without shells, eggs with soft shells, eggs with rough shells, torsion of the oviduct, systemic infections, infections of the reproductive tract, and genetic factors (Krautwald-Junghanns et al., Vet Rec. 1998, 143:498-502, see particularly the left column of page 499). Cloacal problems, such as cloacal prolapse, can be caused by infection with *Cryptosporidium* (Penrith et al., Onderstepoort J Vet Res. 1994, 61:283-289). Further, cloacal prolapse is known to occur in male birds, and note that egg production and laying are not observed in males (Ibid). Given that many of the diseases recited as reproductive diseases and disorders are caused by microbial infections or physical abnormalities, it is unclear how generation of an anti-ZP protein antibody response in such animals would be of therapeutic benefit.

Therefore, given the breadth of applicant's claimed invention, the lack of a working example comprising administration of a composition comprising both avian and non-avian ZP proteins to a bird, the fact that many of the recited reproductive diseases and disorders are caused by factors not directly linked to egg production or laying, and the fact that administration of ZP proteins often causes the reproductive disease ovarian autoimmunity, a skilled artisan would be unable to practice the breadth of applicant's claimed method without conducting undue research.

Claim Rejections - 35 USC § 103

9. Claims 4, 6, 12-15, 17, 18, 21, 23, 27-29, 41, 42, and 44-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Curtiss et al. (US Patent 5,656,488, of record) in view of Harris et al. (US Patent 5,976,545) in view of Mahi-Brown et al. (Birth Control Vaccines, 1995, pages 41-61) and in view of Waclawek et al. (Biology of Reproduction, 1998, 59:1230-1239).

Curtiss et al. teach reducing or preventing fertilization of eggs in birds by administering a glycoprotein, ZP3, from pigs (see entire document, particularly the paragraph spanning columns 2 and 3, lines 11-22 of column 7). They teach that the administered glycoprotein is naturally occurring, recombinantly made, is to be administered with or without carriers (i.e. avirulent microbes) that are dually functional

(since the microbe acts as a carriers and as an immunogen), and is administered with or without adjuvants such as aluminum hydroxide (see particularly lines 44-65 of column 3 and lines 10-34 of column 16). Curtiss et al. further teach that their compositions when administered elicit antibody responses, and as such the compositions minimally comprise B cell epitopes. These teachings differ from the instant claimed invention in that Curtiss et al. do not teach administering a composition comprising non-avian and avian ZP proteins to a bird.

Harris et al. teach the sequence of ZP proteins from numerous animals, and teach that the ZP proteins administered to an animal must be capable of eliciting an antibody response that reacts with the animal's endogenous ZP proteins to be therapeutically effective (see entire document, particularly column 8).

Mahi-Brown et al. teach that administered ZP proteins are not immunogenic when administered to the same species but are often immunogenic when administered to other species (see particularly the bottom of the right column of page 45). However, while administration of porcine ZP proteins elicits an anti-porcine ZP antibody response in non-porcine animals, these elicited antibodies are known not to crossreact with endogenous ZP proteins in all animals (see particularly the second full paragraph of the right column of page 46).

Waclawek et al. teach the purification and protein sequence of chicken ZP3 (see entire document, particularly Figures 2 and 3).

Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to add avian ZP proteins to the compositions administered to birds in the methods taught by Curtiss et al. Motivation to do so comes from the teachings of Harris et al. that elicited antibody responses must be capable of crossreacting with endogenous ZP proteins and the teachings of Mahi-Brown that endogenous ZP proteins are not immunogenic and that porcine ZP does not elicit antibodies that crossreact with endogenous ZP proteins in all animals. As such, the presence of porcine ZP protein in the administered composition would ensure that an immune response was generated while the presence of avian ZP protein would ensure

that some of the elicited antibody response was directed to endogenous avian ZP proteins.

10. Claims 19 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Curtiss et al. (US Patent 5,656,488, of record) in view of Harris et al. (US Patent 5,976,545) in view of Mahi-Brown et al. (Birth Control Vaccines, 1995, pages 41-61) and in view of Waclawek et al. (Biology of Reproduction, 1998, 59:1230-1239) as applied to claims 4, 6, 12-15, 17, 18, 21, 23, 27-29, 41, 42, and 44-47 above, and further in view of Willis et al. (J. Equine Vet Sci, 1994, 14:364-370).

The claimed invention differs from the teachings of Curtiss et al., Harris et al., Mahi-Brown et al., and Waclawek et al., in the recitation that the administered composition comprises the adjuvant STDCM.

Willis et al. teach the use of STDMC in methods of vaccinating animals with ZP proteins (see entire document, particularly the first paragraph). STDMC offers an advantage over other adjuvants in that its use does not produce unwanted side effects of vaccination, such as abscess formation at the vaccination site (see particularly the second full paragraph of the left column of page 369).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to substitute STDMC for the adjuvant taught in the methods of Curtiss et al. Harris et al. Mahi-Brown et al., and Waclawek et al. Motivation to make this substitution comes from the teachings of Willis et al. that STDMC offers advantages over other adjuvants in that the use of STDMC does not lead to abscess formation at the vaccination site.

Claim Objections

11. Claims 23 and 41 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim, or amend the claim to place the claim in proper dependent form, or rewrite the claim in independent form.

Specifically, applicant has amended independent claim 4 to recite the limitations of dependent claim 41 and has retained claim 41. As such, claim 41 adds no additional limitations to the recited method.

Further, claim 23 recites that the composition comprises non-avian ZP or a fragment thereof. The presence of non-avian ZP or fragments thereof is a limitation recited in independent claim 4, and as such claim 23 does not further limit the claimed invention.

12. No claims are allowable.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is 571-272-2934. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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September 7, 2006

9/14/06
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